

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF ALBERTA]

Some 1,3-Diphenylpropylamines

BY ROBERT G. CHRISTIANSEN, RAYMOND R. BROWN, ALLAN S. HAY, ALEX NICKON AND REUBEN B. SANDIN

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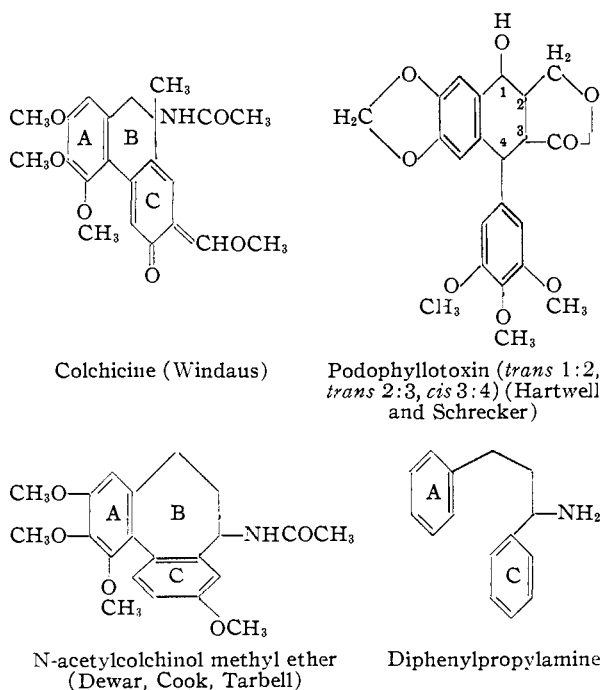
The preparation of a series of 1,3-diphenylpropylamines is described. These compounds have been prepared for testing for their effectiveness against Sarcoma 37 of which the results have been published elsewhere. In the preparation of the amines, the Leuckart reaction of the hydrochalcones has been found to afford satisfactory yields of relatively pure compounds. In the reduction of substituted alkoxy oximes to amines it has been observed that sodium and alcohol leads to replacement of hindered methoxyl groups by hydrogen. This has not been observed when sodium amalgam and alcohol is used or when catalytic hydrogenation is carried out.

Colchicine is a powerful mitotic poison and this fact has led to a study of the action of colchicine and structurally related compounds on mammalian cancer. Downing, Hartwell, Leiter and Shear¹ have found that a number of these compounds are potent in damaging Sarcoma 37. Derivatives of diphenylethylamine which are based on the original Windaus structure² for colchicine have been made by Lettré and Fernholz³ and were found to possess the ability to inhibit the mitosis of certain cells in tissue culture. Hartwell and co-workers^{1,4} have also prepared a variety of α,β -diphenylethylamines and have found many of them to be potent in damaging Sarcoma 37. The Windaus structure for colchicine has been shown to be in error and it has now been demonstrated that both rings B and C are

seven-membered.⁵ Based on the structure of a compound such as colchinal methyl ether in which ring B is a seven-membered ring the present authors have prepared some alkoxy-substituted 1,3-diphenylpropylamines.

The method chosen for the preparation of the substituted diphenylpropylamines was the aldol condensation of the appropriate aldehyde and ketone to form the chalcone, followed by the reduction to the hydrochalcone, oximation and final reduction to the amine. In a number of cases it was found advantageous to convert the hydrochalcone directly to the amine by the Leuckart reaction. A typical reaction sequence is shown in Chart I.

Only new compounds are reported in this work. New chalcones were prepared in the usual manner from 3,4,5-trimethoxybenzaldehyde (I) and 3-hydroxyacetophenone, and from 3,5-dimethoxyacetophenone and piperonal. Hydrochalcones were prepared by the direct reduction of the chalcones. The oximation of the hydrochalcones appeared to give one geometrical isomer in every case, judging by yields and purity of the oximes. The oximes were reduced to the amines by sodium amalgam and alcohol or by sodium in boiling absolute alcohol. In the case of the oxime of 3,4,5-trimethoxy-3'-hydroxyhydrochalcone high pressure hydrogenation with Raney nickel afforded a high yield of very pure amine. The Leuckart reaction of the hydrochalcones usually gave good yields of the amines directly. However, with 3,4,5-trimethoxy-3'-hydroxychalcone the Leuckart reaction was impossible.⁶ When the oxime of 3',4',5'-trimethoxy-3,4-methylenedioxyhydrochalcone was reduced with sodium in boiling absolute alcohol, the 4'-methoxy group (see Chart I) was replaced by hydrogen. The literature contains numerous references to the replacement of alkoxy groups when various reducing agents have been allowed to react on substituted alkyl aryl ethers.⁷ However in the work carried out by Hartwell and Kronberg⁴ and by the present authors, there was no indication of alkoxy displacement when sodium amalgam and alcohol was used as the reducing agent in the preparation of amines from alkoxy substituted oximes.



(1) V. Downing, J. L. Hartwell, J. Leiter and M. J. Shear, *Can. Research*, **9**, 598 (1949). See also J. Leiter, V. Downing, J. L. Hartwell, and M. J. Shear, *J. Nat. Cancer Inst.*, **13**, 379 (1952). It is also interesting to note that Helen M. Dyer in her comprehensive "An Index of Tumor Chemotherapy" published March 1949 by the Federal Security Agency, Public Health Service, lists almost fifty references to colchicine.

(2) A. Windaus, *Ann.*, **439**, 59 (1924).

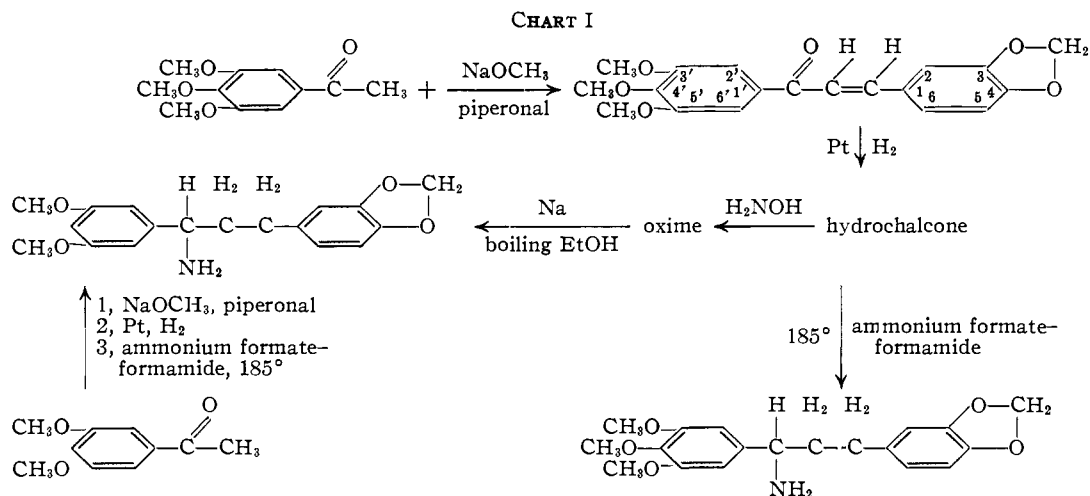
(3) (a) H. Lettré and H. Fernholz, *Z. physiol. Chem.*, **278**, 175 (1943); (b) H. Lettré, *Can. Research*, **12**, 827 (1952).

(4) J. L. Hartwell and S. R. I. Kornberg, *THIS JOURNAL*, **67**, 1606 (1945).

(5) M. J. S. Dewar, *Nature*, **155**, 141 (1945); A. Cohen, J. W. Cook and E. M. F. Roe, *J. Chem. Soc.*, 194 (1940); N. Barton, J. W. Cook and J. D. Loudon, *ibid.*, 176 (1945); H. R. V. Arnstein, D. S. Tarbell, H. T. Huang and G. P. Scott, *THIS JOURNAL*, **70**, 1669 (1948); H. Rapoport, A. R. Williams and M. E. Cisney, *ibid.*, **72**, 3324 (1950).

(6) M. L. Moore in R. Adams, "Organic Reactions," Vol. V, John Wiley and Sons, Inc., New York, N. Y., 1949, p. 311.

(7) S. Kostanecki and V. Lampe, *Ber.*, **41**, 1327 (1908); F. W. Semmler, *ibid.*, **41**, 2556 (1908); E. Schwenk, D. Papa, B. Whitman and H. Ginsberg, *J. Org. Chem.*, **9**, 1 (1944).



Through the kindness of Dr. J. L. Hartwell it was possible to have the diphenylpropylamines tested for their effectiveness against Sarcoma 37. The results of this work have recently been published.⁸ It is interesting that seven of these compounds showed activity in damaging Sarcoma 37, but a dose near the maximum tolerated was required. Negative results with a small number of diphenylpropylamines have been reported by Lettré and co-workers^{9,9} and by Skipper, *et al.*¹⁰ It is also of interest that three of the compounds reported in the present work are the diphenylpropylamines that would result if the B-ring were opened in colchinal, colchinal methyl ether and N-acetylcolchinal methyl ether (compounds 24, 22 and 23, Table II). Moreover compounds (19 and 21, Table II) contain the methylenedioxy group. Compound 19 contains in addition the trimethoxyphenyl group. The present authors considered these groups to be important in view of the fact that they are also present in such compounds as podophyllotoxin. The interesting work of Leiter, Downing, Hartwell and Shear¹¹ has shown that podophyllotoxin has tumor-damaging properties.¹²

Experimental

Aldehydes.—2,3-Dimethoxybenzaldehyde, anisaldehyde, veratraldehyde and piperonal were the best grades available from the Eastman Kodak Company. 3,4,5-Trimethoxybenzaldehyde was prepared according to the procedure outlined by Buchanan, Cook and Loudon.¹³

Ketones.—*p*-Methoxyacetophenone was obtained from the Eastman Kodak Company. 3-Hydroxyacetophenone was prepared from 3-aminoacetophenone by diazotization and hydrolysis in the usual manner. Methylation of 3-hydroxyacetophenone afforded 3-methoxyacetophenone in

good yield. 3-Nitroacetophenone was best prepared by the method developed by Cobb.¹⁴ Hydrogenation of 3-nitroacetophenone in ethyl acetate at 50 p.s.i. (room temperature) with Adams platinum oxide catalyst afforded a high yield of pure 3-aminoacetophenone, m.p. 93–94°. 3,4,5-Trimethoxyacetophenone¹⁵ was prepared without difficulty from 3,4,5-trimethoxybenzoyl chloride and dimethylcadmium.¹⁶ 2,3,4-Trimethoxyacetophenone was prepared by the procedure of Buu-Hoi and Cagniant.¹⁷ 3,5-Dimethoxybenzoic acid was obtained by methylating¹⁸ the dihydroxy acid.¹⁹ 3,5-Dimethoxyacetophenone was obtained in satisfactory yield from 3,5-dimethoxybenzoyl chloride and dimethylcadmium.^{16,20}

Chalcones (Table I).—The substituted chalcones were produced by condensing equimolar amounts of aldehyde and ketone in methanol with sodium methoxide as catalyst. The condensation occurred best in the cold and afforded a high yield of easily purified yellow, crystalline chalcone. The chalcones corresponding to amines 11,²¹ 13,²² 15,²³ 16,^{3(a)} 18,^{15,24} 25^{15,24} (Table II) were known compounds.

Hydrochalcones (Table I).—The hydrochalcones were prepared by the low pressure (50 p.s.i.) hydrogenation of the chalcones dissolved in ethyl acetate. Adams platinum oxide catalyst was used and in all cases the pressure drop corresponded to the theoretical. When hydrogenation was complete, the catalyst was removed by filtration and the solvent was distilled under reduced pressure. This afforded a white hydrochalcone which was crystallized from ethanol. Hydrochalcones corresponding to amines 11,²¹ 13,²² 15,²⁶ 18^{15,24} and 25^{15,24} (Table II) have been recorded before.

Hydrochalconeoximes (Table I).—Oximation of the hydrochalcone was carried out by refluxing the hydrochalcone for five hours, with a slight excess of hydroxylamine hydrochloride in an equal volume mixture of ethanol and pyridine.²⁶ This reaction mixture was poured into ice and water which afforded the solid oxime which was crystallized from

(8) J. Leiter, J. L. Hartwell, I. Kline and M. J. Shear, *J. Nat. Cancer Inst.*, **14**, 645 (1953).

(9) (a) H. Lettré, *Ang. Chem.*, **63**, 421 (1951); (b) H. Lettré and E. Hartwig, *Z. physiol. Chem.*, **291**, 164 (1952).

(10) H. E. Skipper, M. Bell and J. B. Chapman, *Cancer*, **4**, 360 (1951).

(11) J. Leiter, V. Downing, J. L. Hartwell and M. J. Shear, *J. Nat. Cancer Inst.*, **10**, 1273 (1950).

(12) For recent important work on the structure of podophyllotoxin see N. L. Drake and E. H. Price, *This Journal*, **73**, 201 (1951); J. L. Hartwell and A. W. Schrecker, *ibid.*, **73**, 2909 (1951); A. W. Schrecker and J. L. Hartwell, *ibid.*, **75**, 5916 (1953). In view of the biologic activity of podophyllotoxin it might be worthwhile to investigate alkoxy 1,4-diphenylbutylamines.

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(14) E. C. Cobb, *Proc. S. Dakota Acad. Sci.*, **25**, 64 (1945).

(15) V. J. Harding, *J. Chem. Soc.*, **105**, 2790 (1914).

(16) For an excellent review of the use of organocadmium reagents for the preparation of ketones see J. Cason, *Chem. Revs.*, **40**, 15 (1947).

(17) Buu-Hoi and P. Cagniant, *Rec. trav. chim.*, **64**, 214 (1945).

(18) C. Bitlow and G. Riess, *Ber.*, **35**, 3900 (1902); F. Mauthner, "Organic Syntheses," Coll. Vol. 1, 2nd ed., John Wiley and Sons, Inc., New York, N. Y., 1941, p. 537.

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(20) E. H. Woodruff, *This Journal*, **64**, 2859 (1942); H. Gilman and J. F. Nelson, *Rec. trav. chim.*, **55**, 518 (1936).

(21) P. Pfeiffer, G. Armbruster, P. Backes and H. Oberlin, *J. prakt. Chem.*, **108**, 341 (1924).

(22) V. Tognazzi, *Gazz. chim. ital.*, **54**, 697 (1924).

(23) R. Dickinson, I. M. Heilbron and F. Irving, *J. Chem. Soc.*, 1888 (1927).

(24) G. Bargellini and L. Monti, *Gazz. chim. ital.*, **44**, 25 (1914).

(25) P. Pfeiffer, E. Kalckbrenner, W. Kunze and K. Levin, *J. prakt. Chem.*, **119**, 109 (1928).

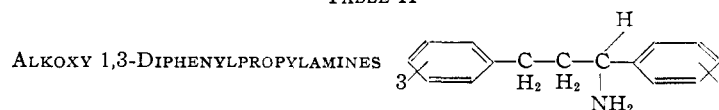
(26) I. Allen and J. S. Buck, *This Journal*, **52**, 312 (1930).

TABLE I
INTERMEDIATE COMPOUNDS

Com- pound	Name	Appearance, solv.	M.p., °C. (uncor.)	Yield, crude, %	Formula	Analyses, %			
						Carbon		Hydrogen	
						Calcd.	Found	Calcd.	Found
Chalcone									
1	3'-Hydroxy-3,4,5-trimethoxy-	Yellow crystals, alc.	173-174	87	C ₁₈ H ₁₆ O ₅	68.8	68.3	5.8	5.9
2	3',5'-Dimethoxy-3,4-methylenedioxy-	Pale yellow needles, alc.	123	87	C ₁₈ H ₁₆ O ₅	69.2	68.6	5.2	5.4
Hydrochalcone									
3	4',3,4,5-Tetramethoxy- ^b	White needles, alc.	94-95	77	C ₁₉ H ₂₂ O ₅	69.1	68.9	6.7	6.6
4	3'-Hydroxy-3,4,5-trimethoxy-	White crystals, alc.	140-140.5	90	C ₁₈ H ₂₀ O ₅	68.3	68.4	6.4	6.5
5	3',3,4,5-Tetramethoxy- ^a	White plates, alc.	69-70	80	C ₁₉ H ₂₂ O ₅	69.1	68.4	6.7	6.8
6	3',5'-Dimethoxy-3,4-methylenedioxy-	Colorless needles, alc.	76-77	85	C ₁₈ H ₁₈ O ₅	68.8	68.3	5.8	6.0
Hydrochalcone oxime									
7	4',3,4,5-Tetramethoxy- ^b	White needles, alc.	101-102	81	C ₁₉ H ₂₃ O ₅ N	66.1	66.2	6.7	6.8
8	3'-Hydroxy-3,4,5-trimethoxy-	White crystals, alc.	131-132	90	C ₁₈ H ₂₁ O ₅ N	65.3	65.3	6.4	6.8
9	2',3',4'-Trimethoxy-3,4-methylenedioxy-	White crystals, alc.	110-111	61	C ₁₉ H ₂₁ O ₅ N	63.5	63.3	5.9	5.9
10	3',4',5'-Trimethoxy-3,4-methylenedioxy-	White crystals, alc.	108-109	77	C ₁₉ H ₂₁ O ₅ N	63.5	63.2	5.9	6.1

^a Prepared by the methylation of hydrochalcone 4. See ref. 9b. ^b This compound has been reported but no analysis is given. See ref. 3a.

TABLE II



Com- pound	1-Phenyl	Substituents on 3-Phenyl	Derivative	M.p., °C. (uncor.)	Yield crude, %	Formula	Analyses, %			
							Carbon		Hydrogen	
							Calcd.	Found	Calcd.	Found
11	4-Methoxy	2,3-Dimethoxy	Hydrochloride	202-203	59 ^a	C ₁₈ H ₂₄ O ₃ NCl	64.0	63.7	7.2	7.4
12	4-Methoxy	2,3-Dimethoxy	Picrate	157-158	37 ^b	C ₂₄ H ₂₆ O ₁₀ N ₄	54.3	54.8	4.9	5.1
13	4-Methoxy	4-Methoxy	Picrate	168-169	69 ^a , 81 ^b	C ₂₃ H ₂₄ O ₉ N ₄	55.2	55.6	4.8	5.2
14	4-Methoxy	4-Methoxy	Hydrochloride	185-186		C ₁₇ H ₂₂ O ₂ NCl	66.2	66.1	7.2	7.4
15	None	3,4-Dimethoxy ⁱ	Picrate	127-129	57 ^a , 88 ^b	C ₂₃ H ₂₄ O ₉ N ₄	55.2	55.3	4.8	5.2
16	4-Methoxy	3,4,5-Trimethoxy ^{a,i}	Hydrochloride	192-193	75 ^b	C ₁₉ H ₂₆ O ₄ NCl	62.0	61.9	7.1	7.1
17	4-Methoxy	3,4,5-Trimethoxy	N-Acetyl	85-86		C ₂₁ H ₂₇ O ₅ N	67.5	67.8	7.3	7.6
18	3,4,5-Trimethoxy	3,4-Methylenedioxy	Picrate	150-151	52 ^{b,d}	C ₂₅ H ₂₆ O ₁₂ N ₄	52.3	52.1	4.6	5.0
19	3,4,5-Trimethoxy	3,4-Methylenedioxy	Hydrochloride	201-202	57 ^{b,d}	C ₁₉ H ₂₄ O ₅ NCl ⁱ	59.8	59.6	6.3	6.6
20	None	3,4-Methylenedioxy	Picrate	218-219	40 ^{b,d}	C ₂₂ H ₂₆ O ₉ N ₄	54.5	54.9	4.1	4.6
21	None	3,4-Methylenedioxy	Hydrochloride ^e	173-174		C ₁₆ H ₁₉ O ₂ NCl ^j				
22	3-Methoxy	3,4,5-Trimethoxy	Hydrochloride	195-196	56 ^{b,d}	C ₁₉ H ₂₆ O ₄ NCl ^k				
23	3-Methoxy	3,4,5-Trimethoxy ^m	N-Acetyl	92-93		C ₂₁ H ₂₇ O ₅ N	67.5	67.6	7.3	7.5
24	3-Hydroxy	3,4,5-Trimethoxy		193-194	80 ^f	C ₁₈ H ₂₃ O ₄ N	68.0	68.1	7.4	7.3
25	2,3,4-Trimethoxy	3,4-Methylenedioxy	Picrate ^g	158-159	38 ^b	C ₂₅ H ₂₆ O ₁₂ N ₄	52.3	52.4	4.6	4.8
26	3,5-Dimethoxy	3,4-Methylenedioxy	Picrate	185-187	35 ^{d,h}	C ₂₄ H ₂₄ O ₁₁ N ₄	52.9	52.4	4.4	4.5

^a Amine prepared by the sodium and alcohol reduction of the oxime. ^b Amine prepared by the Leuckart reaction. ^c When the oxime was reduced with sodium and alcohol the hydrochloride melted at 188-189°, and the analysis indicated that one methoxyl group had been removed and substituted by hydrogen. *Anal.* Calcd. for C₁₈H₂₄O₃NCl: C, 64.0; H, 7.2. Found: C, 63.9; H, 7.4. ^d Yield of pure compound. ^e Prepared from picrate. ^f Amine prepared by high pressure (1000 p.s.i.) hydrogenation of the oxime in ethanol at 85° for one hour with Raney nickel as catalyst. The amine was also prepared by the sodium amalgam reduction of the oxime, and there was no indication of methoxyl displacement. ^g When the amine was made by the sodium and alcohol reduction of the oxime, the picrate melted at 157-159°, yield 50%. However a mixed m.p. determination of this picrate and the picrate from the Leuckart reaction showed as much as four degrees depression. *Anal.* Calcd. for C₂₅H₂₆O₁₂N₄: C, 52.3; H, 4.6. Found: C, 52.4; H, 4.8. ^h Amine prepared by the sodium-alcohol reduction of oxime 10 (Table I). The same picrate was obtained when the Leuckart reaction was carried out on hydrochalcone 6 (Table I). An equal part mixture of the two picrates showed no m.p. depression. Moreover the two amines afforded 3,5-dimethoxybenzoic acid, m.p. 179-182°, on oxidation with potassium permanganate. ⁱ *Anal.* Calcd. for C₁₉H₂₄O₅NCl: Cl, 9.6. Found: Cl, 9.3, 9.3. ^j *Anal.* Calcd. for C₁₆H₁₉O₂NCl: Cl, 12.2. Found: Cl, 12.4, 11.8. ^k *Anal.* Calcd. for C₁₉H₂₆O₄NCl: Cl, 9.6. Found: Cl, 9.3. ^l The N-acetyl derivative has been reported. See ref. 3a. ^m The oxalate of this amine has been reported. See ref. 9b.

ethanol. The oximes corresponding to the amines 11, 13, 15²⁸ (Table II) have been reported before.

1,3-Diphenylpropylamines (Table II).—The procedure for the reduction of the oximes using sodium amalgam was that of Hartwell and Kornberg.⁴ When the sodium and alcohol reduction was carried out, small pieces of sodium

were added to a refluxing solution of the oxime in absolute alcohol. The reaction mixture was cooled, diluted with water and extracted with benzene. The extract was dried over sodium sulfate and the benzene removed under reduced pressure, which afforded the amine as a light tan colored, viscous oil. This method of reduction could not be

used with 3,4,5-trimethoxyphenyl substituted oximes. The amines were also prepared directly from the hydrochlorides by the Leuckart reaction.²⁷ In all cases reported here (except compound 24, Table II) the free bases could not be obtained crystalline. The hydrochlorides were obtained crystalline as colorless needles when a dried solution of the amine in ether was treated with dry hydrogen chloride. Crystallization from absolute alcohol afforded the pure amine salt. The picrates were prepared by treating a solution of the amine in alcohol with excess picric acid. The yellow crystalline picrates were crystallized from alcohol. When the

(27) A. W. Ingersoll, J. H. Brown, C. K. Kim, W. D. Beauchamp and G. Hennings, *THIS JOURNAL*, **58**, 1808 (1936).

picrate of amine 15 (Table II) was crystallized from absolute alcohol the m.p. was 166–167°. The same picrate crystallized from 50% ethanol melted at 127–129°.

Acknowledgments.—The authors wish to express their gratitude to Dr. Jonathan L. Hartwell of the National Cancer Institute for helpful discussions and continued interest. One of us (R.B.S.) wishes to express his thanks to Dr. Gordon Finlay of Chippawa, Ontario, and to the Canadian Cancer Society for generous financial support of this work.

EDMONTON, ALBERTA, CANADA

[CONTRIBUTION FROM THE RICHARDSON CHEMISTRY LABORATORY, TULANE UNIVERSITY]

The Acid-catalyzed Reaction of Alkyl Azides upon Carbonyl Compounds¹

By J. H. BOYER AND J. HAMER²

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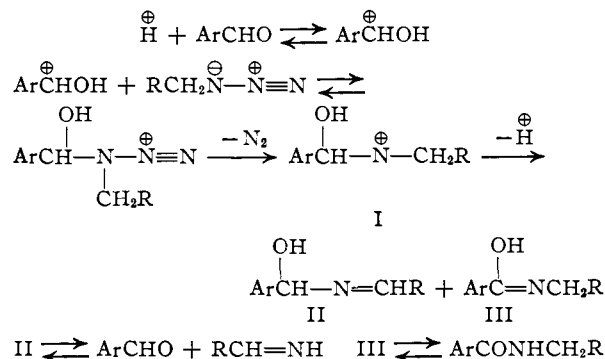
In an extension of the Schmidt reaction, amides were obtained from certain primary azides and aromatic aldehydes. The acid-catalyzed reaction at higher temperatures of β - and γ -azidoaldehydes with aromatic aldehydes brought about the formation of oxazolines and dihydrooxazines, respectively.

The literature has described certain similarities between aliphatic diazo compounds and their isosteric azides. Alkylation of aldehydes and ketones by diazomethane and the corresponding acid-catalyzed reaction of hydrazoic acid upon carbonyl compounds, also known as the Schmidt reaction, provide a good example. This report describes an extension of the latter reaction to alkyl azides.

Whereas diazoethane and higher homologs are more reactive than diazomethane toward carbonyl compounds,³ alkyl azides are not capable of participation in a corresponding acid-catalyzed reaction on certain carbonyl compounds. Thus, no product was identified from the acid-catalyzed decomposition of methyl azide in the presence of benzoic acid.⁴ Apparently methyl azide also failed to react with acetophenone since the only product identified from the reaction in the presence of sulfuric acid was acetanilide,⁵ obtained in 2% yield.

A general reaction between alkyl azides and carbonyl compounds in the presence of a strong acid now has been demonstrated; from aromatic aldehydes the most encouraging results were obtained. A straight-forward adaptation of the currently accepted mechanism for the Schmidt reaction⁶ and the alkylation of carbonyl compounds by diazoalkanes⁶ provides an explanation for this new route to certain N-substituted amides and derivatives.

The behavior of an alkyl azide as a weak Lewis base toward a carbonium ion is consistent with its reaction with the proton. In the latter case protonation is presumably the first step in the well-known acid-catalyzed decomposition of or-



ganic azides.⁷ From a primary alkyl azide (RCH_2N_3) and the conjugate acid of an aldehyde, apparently an adduct was formed which subsequently underwent the loss of nitrogen, ejection of a proton and rearrangement either by a stepwise procedure such as the one described here or by an operation which would involve the simultaneous loss of nitrogen and the proton. Taft's rule that a carbonium ion loses a proton from the more electron-rich adjacent carbon atom,⁸ was extended to the present system I. It was in excellent agreement with the experimental observation that the formation of amides either failed to occur altogether or occurred only to a minor extent with alkyl azides and aromatic aldehydes. This was to be expected, since amide formation involved removal of the proton from the aryl carbinol carbon atom (electron poor). On the other hand, removal of the proton from the adjacent alkyl carbon (electron rich) apparently resulted in the initial formation of a hydroxy Schiff base II and subsequent degeneration into an aldehyde and imine. The tautomeric shifts necessary to isomerize the hydroxy Schiff base II into the thermodynamically more stable amide modification are

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(2) Research Associate, 1953–1954.

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(5) P. A. S. Smith, *THIS JOURNAL*, **70**, 320 (1948).

(6) E. A. Alexander, "Ionic Organic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1950, p. 51.

(7) K. W. Sherk, A. G. Houpt and A. W. Brown, *THIS JOURNAL*, **62**, 329 (1940); M. S. Newman and H. L. Goldenhorn, *ibid.*, **70**, 317 (1948); J. H. Boyer and F. C. Canter, *Chem. Revs.*, **54**, 1 (1954); P. A. S. Smith and B. B. Brown, *THIS JOURNAL*, **73**, 2438 (1951).

(8) R. W. Taft, Jr., *ibid.*, **70**, 3364 (1948).